What is claimed is:

- 1. A method for identifying at least one agent which modulates a preselected biological condition controlled by the circadian clock in a subject comprising
- a) inserting a monitoring device into, or in close proximity to the pineal, causing little or no tissue damage to the non-pineal tissue during the inserting;
- b) monitoring the chemical output of the pineal and monitoring a preselected biological condition of a first subject; and,
- c) monitoring the chemical output of the pineal and monitoring the same preselected biological condition as in step b) in a second subject after contacting the second subject with the at least one agent;

wherein an alteration in the chemical output of the pineal and in the preselected biological condition in the second subject as compared to the chemical output of the pineal and preselected biological condition in the first subject identifies at least one agent which modulates a preselected biological condition controlled by the circadian clock.

- 2. The method of claim 1, wherein the monitoring of the chemical output is selected from the group consisting of *in vivo* microdialysis and *ex vivo* monitoring.
- 3. The method of claim 2, wherein the monitoring the chemical output comprises monitoring output of melatonin or serotonin (5-HT) or both.
- 4. The method of claim 1, wherein the preselected biological condition is subject behavior.
- 5. The method of claim 4, wherein the subject behavior is selected from the group consisting of symptoms of adaptation to new time zones, symptoms resulting from jet lag, symptoms of frequent shift work sleep abnormalities and symptoms of seasonal affective illnesses.

- 6. The method of claim 5, wherein the symptom is selected from the group consisting of a change in hormone secretion, a change in melatonin output, a change in sleep patterns, a change in activity patterns, a change in cortisol secretion and a change in core body temperature.
- 7. The method of claim 1, wherein the preselected biological condition is cellular expression of at least one biological molecule of interest.
- 8. The method of claim 1, wherein the preselected biological condition is tissue physiology.
- 9. The method of claim 1, wherein the monitoring is continuous, periodic, short term, long term, or any combination thereof.
- 10. The method of claim 1, wherein the monitoring is of a length of time sufficient to monitor one or more circadian rhythms of the subject.
- 11. The method of claim 1, wherein the first subject and the second subject are the same individual.
- 12. A composition comprising one or more agents and derivatives thereof identified by the method of claim 1.
- 13. An agent or derivative thereof identified by the method of claim 1 in purified form.
- 14. A pharmaceutically acceptable composition comprising one or more agents, or derivatives thereof, identified by the method of claim 1.
- 15. An improved method of carrying out surgery on the pineal comprising opening the skull of a subject and inserting a monitoring device, the improvement comprising a circular dental disk drill to open the skull, and a hook to lift and/or

1-WA/2164296.2

separate nonpineal tissues away from the pineal to allow visual placement of the monitoring device into, or in close proximity to, the pineal, causing little or no tissue damage to the non-pineal tissue during the inserting.

- 16. The method of claim 15, wherein the monitoring device is a microdialysis probe.
- 17. A method for implantation of a microdialysis probe for monitoring of chemicals produced by the pineal, comprising opening the skull and separating nonpineal tissue away from the pineal so as to visually expose the pineal, implanting a microdialysis probe into, or in close proximity to, the pineal, causing little or no tissue damage to the non-pineal tissue during the implanting.
- 18. A method for monitoring the presence of at least one chemical in the chemical output of the pineal comprising
- a) opening the skull and visually exposing the pineal;
- b) inserting a microdialysis probe into, or in close proximity to, the pineal, wherein non-pineal tissue exhibits little or no damage from the inserting;
- c) contacting the pineal or the subject with at least one chemical; and,
- d) monitoring the chemical output of the pineal for presence of the same or different chemical by *in vivo* microdialysis.
- 19. The method of claim 18, wherein the monitoring is long term, short term, continuous or periodic or any combination thereof.
- 20. A method of modulating a preselected condition controlled by the circadian clock in a subject in need thereof comprising
- a) monitoring time of onset of melatonin secretion from said subject prior to presenting a light pulse to said subject;
- b) presenting at least one light pulse to said subject, wherein said light pulse is presented during the subject's subjective night phase;

- c) monitoring time of onset of melatonin secretion from said subject after said light pulse; wherein when said melatonin secretion exhibits a shift in the time of onset of secretion after presentation of said light pulse, said preselected condition has been modulated.
- 21. The method of claim 20, wherein said light pulse is presented during the earlier half of the subjective night phase.
- 22. The method of claim 20, wherein said light pulse is presented during the later half of the subjective night phase.
- 23. The method of claim 20, wherein said preselected condition is selected from the group consisting of a change in hormone secretion, a change in melatonin output, a change in sleep patterns, a change in activity patterns, a change in cortisol secretion and a change in core body temperature.